PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Graeme I. Bell
Kazuya Yamagata
Naohisa Oda
Pamela J. Kaisaki
Hiroto Furuta
Yukio Horikawa
Stephan Menzel

Serial No.: Unknown

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For: MUTATIONS IN THE DIABETES SUSCEPTIBILITY GENES HEPATOCYTE NUCLEAR FACTOR (HNF) 1 ALPHA (α), HNF-1β AND HNF-4α

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PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

Sir:

Please amend this application as follows:

In The Specification

At page 2, line 1, insert the following:

--This is a continuation of co-pending application Serial No. 08/927,219, filed September 9, 1997, and claims priority to provisional application 60/029,679, filed October 30, 1996, provisional application 60/028,056, filed October 2, 1996, and provisional application 60/025,719, filed September 10, 1996.--

In the Claims

Cancel claims 1-15, 17, and 41-62, without prejudice.

Please amend the claims as follows:

16. (Amended) A method of regulating diabetes in an animal comprising [the step of modulating HNF function in the animal] diagnosing diabetes in the animal via analysis of an HNF-encoding nucleic acid sequence for a mutation and regulating the diabetes.

18. (Amended) The method of claim [17] 16, wherein the HNF-encoding sequence is an HNF1α-encoding sequence.

19. (Amended) The method of claim [17] 16, wherein the HNF-encoding sequence is an HNF4α-encoding sequence.

20. (Amended) The method of claim [17] 16, wherein the HNF-encoding sequence is an HNF1β-encoding sequence.

21. (Amended) The method of claim 16, wherein [the step of] regulating the diabetes comprises modulating HNF function [comprises] in the animal by providing an HNF polypeptide to the animal.

28. (Amended) The method of claim 26, wherein the expression of an HNF polypeptide [encoded] is induced by providing a nucleic acid [provided] encoding said HNF polypeptide to the animal [is induced].

31. (Amended) The method of claim 16, [wherein] further comprising the step of modulating HNF function in the animal [comprises] by providing a modulator of HNF function to the animal.

Please add the following claims:

--63. The method of claim 28, further comprising providing a nucleic acid encoding an HNF1α polypeptide to the cell.

64. The method of claim 28, further comprising providing a nucleic acid encoding an HNF1β polypeptide to the cell.

65. The method of claim 28, further comprising providing a nucleic acid encoding an HNF4α polypeptide to the cell.

66. The method of claim 26, wherein the provision of an HNF polypeptide is accomplished by stimulating or enhancing expression of the virally-encoded HNF polypeptide.

67. The method of claim 66, wherein the expression of the virally-encoded HNF1α polypeptide is stimulated or enhanced.

68. The method of claim 66, wherein the expression of the virally-encoded HNF1β polypeptide is stimulated or enhanced.

69. The method of claim 66, wherein the expression of the virally-encoded HNF4α polypeptide is stimulated or enhanced.

70. The method of claim 21, wherein the provision of an HNF polypeptide is accomplished by stabilizing the expressed HNF polypeptide.

71. The method of claim 29, wherein the HNF-encoding nucleic acid is introduced to the animal via viral infection.

72. The method of claim 71, further comprising encapsulating the expression construct in a viral particle that will deliver a replicating or non-replicating nucleic acid.

73. The method of claim 72, wherein the viral particle is further defined as an HSV vector.

74. The method of claim 29, wherein the HNF-encoding nucleic acid is introduced to the animal via cultured mammalian cells transfected with the HNF-encoding nucleic acid.

75. The method of claim 74, wherein the mammalian cells are transfected with expression constructs comprising the HNF-encoding nucleic acid by calcium phosphate precipitation, DEAE-dextran, electroporation, direct microinjection, DNA-loaded liposomes, lipofectamine-DNA complexes, cell sonication, gene bombardment using high velocity microprojectiles or receptor-mediated transfection.

76. The method of claim 75, wherein the cells are transfected by DNA-loaded liposomes.

77. The method of claim 76, wherein the liposome is complexed with a hemagglutinating virus.

78. The method of claim 76, wherein the liposome is complexed or employed in conjunction with nuclear non-histone chromosomal proteins.

79. The method of claim 76, wherein the liposome is complexed or employed in conjunction with a hemagglutinating virus and nuclear non-histone chromosomal proteins.

80. The method of claim 76, wherein the liposome is complexed with a ligand.

81. The method of claim 75, wherein the cells are transfected by receptor-mediated transfection.

82. The method of claim 81, wherein the receptor-mediated transfection comprises contacting the cells with receptor-mediated gene targeting vehicles comprising a cell receptor-specific ligand and a DNA-binding agent.

83. The method of claim 82, wherein the ligand is asialoorosomucoid, synthetic neoglycoprotein, mannose, transferrin, CD5, CD22, CD25 or MAA.

84. The method of claim 16, wherein regulating the diabetes comprises increasing insulin secretion.

85. The method of claim 33, wherein the modulator of HNF function is an antisense nucleic acid that will hybridize to the mutated HNF1α gene.

86. The method of claim 34, wherein the modulator of HNF-function is an antisense nucleic acid that will hybridize to the mutated HNF1α gene transcript.

87. The method of claim 36, wherein the modulator of HNF function is an antisense nucleic acid that will hybridize to the mutated HNF4α gene.

88. The method of claim 37, wherein the modulator of HNF-function is an antisense nucleic acid that will hybridize to the mutated HNF4α gene transcript.

89. The method of claim 39, wherein the modulator of HNF function is an antisense nucleic acid that will hybridize to the mutated HNF1β gene.

90. The method of claim 40, wherein the modulator of HNF-function is an antisense nucleic acid that will hybridize to the mutated HNF1β gene transcript.

91. The method of claim 31, wherein the modulator of HNF-function is a mutated HNF-binding protein or peptide.

92. The method of claim 91, wherein the modulator of HNF-function is further defined as a peptidomimetic or antibody that binds immunologically to a mutated HNF1α, HNF1β, or HNF4α.

93. The method of claim 31, wherein the modulator of HNF-function is an antagonist of HNF1α, HNF1β, or HNF4α.

94. The method of claim 31, wherein the modulator of HNF-function is an agent that binds to a mutated HNF1α, HNF1β, or HNF4α target.

95. The method of claim 31, wherein the modulator of HNF function post-translationally modulates DNA-binding activity of HNF4α.

96. The method of claim 95, wherein the DNA-binding activity is modulated by tyrosine phosphorylation of HNF4α.

97. The method of claim 36, wherein the modulator is DCoH.--

REMARKS

Claims 1-15, and 41-62 are canceled herein as drawn to non-elected inventions. Claim 17 is canceled herein as the subject matter therein has been incorporated into claim 16. Claims 16, 18-21, 28, and 31 have been amended to clarify the subject matter of the invention. Claims 63-97 have been added herein. The active claims in this case are claims 16, 18-40 and 63-97. The currently pending claims are attached hereto as Appendix A.

Support for the added claims can be found throughout the specification. More specifically, support for each of the added claims may be found, for example, at the following portions of the specification:

Claims 63-65:	page 110, lines 20-23;
Claims 66-70:	page 110, lines 27-29;
Claims 71-73:	page 111, lines 1-5;
Claims 74-75:	page 111, lines 8-15;
Claims 76-80:	page 112, lines 11-20;
Claim 81:	page 112, lines 24-26;
Claims 82-83:	page 113, lines 1-10;
Claim 84:	page 19, lines 12-18;
Claims 85-89:	page 115, lines 24-27;

Claims 90-91: page 115, lines 28-30;

Claims 92-93: page 116, lines 3-7;

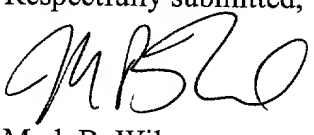
Claims 94-95: page 26, lines 9-15;

Claim 96: page 33, lines 20-29.

The specification has been amended to recite the relationship with the parent case, this application is a continuation of co-pending application Serial No. 08/927,219, filed September 9, 1997, and claims priority to provisional application 60/029,679, filed October 30, 1996, provisional application 60/028,056, filed October 2, 1996, and provisional application 60/025,719, filed September 10, 1996.

It is believed that no fee is due; however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason, the Commissioner is authorized to deduct said fees from Fulbright & Jaworski Deposit Account No. 50-1212/10007982/01999.

Respectfully submitted,



Mark B. Wilson
Reg. No. 37,259
Attorney for Applicants

FULBRIGHT & JAWORSKI
600 Congress, Suite 2400
Austin, Texas 78701
(512) 418-3000

Date: January 3, 2001

APPENDIX A

16. A method of regulating diabetes in an animal comprising diagnosing diabetes in the animal via analysis of an HNF-encoding nucleic acid sequence for a mutation and regulating the diabetes.

18. The method of claim 16, wherein the HNF-encoding sequence is an HNF1α-encoding sequence.

19. The method of claim 16, wherein the HNF-encoding sequence is an HNF4α-encoding sequence.

20. The method of claim 16, wherein the HNF-encoding sequence is an HNF1β-encoding sequence.

21. The method of claim 16, wherein regulating the diabetes comprises modulating HNF function in the animal by providing an HNF polypeptide to the animal.

22. The method of claim 21, wherein the HNF polypeptide is a native HNF polypeptide.

23. The method of claim 22, wherein the native HNF polypeptide is an HNF1α polypeptide that has the sequence of SEQ ID NO: 2.

24. The method of claim 22, wherein the native HNF polypeptide is an HNF4α polypeptide that has the sequence of SEQ ID NO: 79.

25. The method of claim 22, wherein the native HNF polypeptide is an HNF1β polypeptide that has the sequence of SEQ ID NO: 91.

26. The method of claim 21, wherein the provision of an HNF polypeptide is accomplished by inducing expression of an HNF polypeptide.

27. The method of claim 26, wherein the expression of an HNF polypeptide encoded in the animal's genome is induced.

28. The method of claim 26, wherein the expression of an HNF polypeptide is induced by providing a nucleic acid encoding said HNF polypeptide to the animal.

29. The method of claim 21, wherein the provision of an HNF polypeptide is accomplished by a method comprising introduction of an HNF-encoding nucleic acid to the animal.

30. The method of claim 21, wherein the provision of an HNF polypeptide is accomplished by injecting the HNF polypeptide into the animal.

31. The method of claim 16, further comprising the step of modulating HNF function in the animal by providing a modulator of HNF function to the animal.

32. The method of claim 31, wherein the modulator of HNF function is an agonist of HNF1α.

33. The method of claim 31, wherein the modulator of HNF function modulates transcription of an HNF1α-encoding nucleic acid.

34. The method of claim 31, wherein the modulator of HNF function modulates translation of an HNF1α-encoding nucleic acid.

35. The method of claim 31, wherein the modulator of HNF function is an agonist of HNF4α.

36. The method of claim 31, wherein the modulator of HNF function modulates transcription of an HNF4α-encoding nucleic acid.

37. The method of claim 31, wherein the modulator of HNF function modulates translation of an HNF4α-encoding nucleic acid.

38. The method of claim 31, wherein the modulator of HNF function is an agonist of HNF1β.

39. The method of claim 31, wherein the modulator of HNF function modulates transcription of an HNF1β-encoding nucleic acid.

40. The method of claim 31, wherein the modulator of HNF function modulates translation of an HNF1β-encoding nucleic acid.

63. The method of claim 28, further comprising providing a nucleic acid encoding an HNF1α polypeptide to the cell.

64. The method of claim 28, further comprising providing a nucleic acid encoding an HNF1β polypeptide to the cell.

65. The method of claim 28, further comprising providing a nucleic acid encoding an HNF4α polypeptide to the cell.

66. The method of claim 26, wherein the provision of an HNF polypeptide is accomplished by stimulating or enhancing expression of the virally-encoded HNF polypeptide.

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72. The method of claim 71, further comprising encapsulating the expression construct in a viral particle that will deliver a replicating or non-replicating nucleic acid.

73. The method of claim 72, wherein the viral particle is further defined as an HSV vector.

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80. The method of claim 76, wherein the liposome is complexed with a ligand.

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92. The method of claim 91, wherein the modulator of HNF-function is further defined as a peptidomimetic or antibody that binds immunologically to a mutated HNF1α, HNF1β, or HNF4α.

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94. The method of claim 31, wherein the modulator of HNF-function is an agent that binds to a mutated HNF1α, HNF1β, or HNF4α target.

95. The method of claim 31, wherein the modulator of HNF function post-translationally modulates DNA-binding activity of HNF4α.

96. The method of claim 95, wherein the DNA-binding activity is modulated by tyrosine phosphorylation of HNF4α.

97. The method of claim 36, wherein the modulator is DCoH.